

Physiology. — *On the importance of the adrenal glands for the survival of the rat following hypophysectomy.* II. By J. H. GAARENSTROOM and S. E. DE JONGH. (From the Pharmacological Laboratory, Leyden University, Leyden, Holland. (Communicated by Prof. S. T. BOK.)

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Some time ago one of us¹⁾ demonstrated that in hypophysectomized animals the adrenal gland is as indispensable as it is in normal animals. He then announced his intention to estimate the minimum amount of adrenal cortical hormone required to allow hypophysectomized and non-hypophysectomized animals to survive following extirpation of the adrenals.

These experiments were realized but the results could not be interpreted and therefore remained unpublished. Communications by SWANN²⁾ as well as by DEANE and GREEP³⁾ contain views, however, that correspond with our experiments. Therefore we will publish them now.

In a first series of experiments (I) the adrenal gland was removed in four groups of about ten rats each, two groups of which had been hypophysectomized a week before. One hypophysectomized and one normal group were given 0.1 mgm of desoxycorticosterone acetate (doca) daily in 0.2 ccm of oil; the other two groups received 0.2 ccm of oil without doca. Doca was used because it is the pure adrenal cortical hormone that is most easily obtained. The dose, that was administered, was selected in view of its being approximately the minimum amount that unquestionably prolongs the duration of life of adrenalectomized, non-hypophysectomized rats. It appears from the table that following treatment with doca a prolongation of the survival period did actually occur. At the same time, however, it becomes apparent that the animals subjected to both operations did not survive longer than those which were adrenalectomized only, although such a difference might have been anticipated if the need of adrenal cortical hormone were diminished in hypophysectomized rats.

In a next series of experiments (II) the first one was repeated with one modification. It seemed to us that the great number of deaths of hypophysectomized rats shortly after the extirpation of the adrenal gland might have complicated the issue, because these deaths might have to be put down to a generally lowered resistance rather than to a lack of adrenal tissue. Therefore this time all animals were given a single injection of one milligram of doca, immediately following the extirpation of the adrenal gland.

¹⁾ J. H. GAARENSTROOM, Ned. Tijdschr. Geneeskunde **85**, 712 (1941); Acta brevia neerl. **11**, 68 (1941).

²⁾ H. G. SWANN, Physiol. Reviews. **20**, 493 (1940).

³⁾ H. W. DEANE and R. O. GREEP, Am. Journ. Anat. **79**, 117 (1946).

Treatment was continued then in the various groups as it had been in the first series. In the table we may see that the results, thus obtained, were not different in principle.

The mean duration of life of both hypophysectomized groups has been prolonged to a certain extent; it is not surprising that these very groups have profited by the administration of doca following the operation. Again, however, the regular administration of 0.1 mgm of doca do not seem to have had more effect on hypophysectomized animals than it had on animals still possessing a hypophysis.

The mean figures have but a relative value on account of the great spread. In the table the data of the individual animals have been stated as well. Some animals, still surviving after nineteen days (test for remnants of adrenal gland negative) made it necessary to use the sign of > in the mean figures. Nevertheless, the general tendency of the results is obvious and certainly not influenced by spread: Administration of 0.1 mgm of doca gives a survival time of comparable magnitude in hypophysectomized and non-hypophysectomized animals. In our former opinion this result was

TABLE.
Normal

Experimental series	Number of rats	Weight in gm extremes	Treatment	Survival time in days *)	
				of each rat	average
I	10	102—160	oil	5, 6, 7, 7, 7, 7, 8, 8, 10, 10	7.5
	10	104—158	doca	9, 13, 14, 14, 15, 15, 16, 16, 18, >19	>14.9
II	10	108—156	oil **)	4, 7, 7, 8, 8, 8, 9, 9, 10, 10	8.0
	11	116—152	doca **)	2, 3, 7, 9, 11, 11, 13, 18, >19, >19, >19	>11.9
Hypophysectomized					
I	9	95—142	oil	2, 2, 2, 2, 3, 3, 3, 4, 5	3.0
	10	90—152	doca	1, 1, 2, 2, 2, 4, 6, 7, 14, 15	5.6
II	10	114—159	oil **)	3, 3, 4, 4, 4, 4, 4, 5, 5, 6	4.2
	12	112—172	doca **)	1, 1, 4, 4, 4, 6, 8, 12, 12, 13, >19, >19	>8.6

*) From the day of the removal of the adrenal glands on.

***) All animals of the second series were given 1 mgm of doca immediately after the extirpation of the adrenal gland.

past comprehension. It would suggest that hypophysectomized animals need as much adrenal cortical hormone as intact animals do, whereas the size and histologic aspect indicate that the adrenal gland of hypophysectomized animals achieves considerably less, which is more in accordance with the surmise that the need of adrenal cortical hormone has decreased following hypophysectomy. The possibility of the poorly developed adrenal gland of hypophysectomized animals producing, by using its utmost exertions, as much hormone as the normal adrenal gland does with playful ease, was invalidated by the observation that in hypophysectomized animals, too, postoperative rests of the adrenal gland may succeed in keeping the animals alive⁴). Thus a great discrepancy continued to exist which we could not explain, until we heard of the work of SWANN and of that of DEANE and GREEP. In view of their experimental results these authors hold the view that the production of adrenal cortical steroids, comparable with doca (in contradistinction to the supply of the so-called 11-oxysteroids) is not submitted to the influence of corticotropic hormone, and thus is independent of the hypophysis. If the authors mentioned are right we have, our experiments being made with doca, combated an equally great shortage with the same dose in hypophysectomized animals and in intact animals, and thus, in accordance with what may be anticipated in such a case, with equal success. As, conversely, our experiments may be interpreted as a support for the views of both SWANN and DEANE and GREEP, that has been secured by means of quite another method, we proceeded to publish our old data.

Summary.

1. Small amounts of desoxycorticosterone acetate prolong the life of adrenalectomized rats and hypophysectomized-adrenalectomized rats to comparable extents.

2. This result may be linked up with the thesis, published in literature, that the production of doca-like cortical steroids takes place independently of the hypophysis.

⁴) J. H. GAARENSTROOM, *ibid.*